LETTER TO THE EDITOR ON "ROLE OF PERIARTICULAR LIPOSOMAL BUPIVACAINE INFILTRATION IN PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY - A META-ANALYSIS OF COMPARATIVE TRIALS"

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Thanks to Singh and co-authors[1] for their meta-analysis addressing a controversial topic. Post-operative pain control protocols following total knee arthroplasty (TKA) are essential to successful outcomes, with peri-articular injections (PAIs) being an important component. Liposomal bupivacaine (Exparel) is claimed to provide a slow release of local anesthetic, for approximately 72 hours, and has been promoted as a superior component of PAI. Since its introduction, numerous studies show contradicting efficacy. A meta-analysis could provide a substantial amount of clarity. Unfortunately, your study methodology has numerous flaws, which render the conclusions invalid.

Literature on liposomal bupivacaine compares different analgesic techniques. In your paper, you grouped these into 1) infiltration, 2) femoral nerve block, 3) multimodal pain-management. In your analysis, you examined them both separately and together, however the study's conclusions were derived from the ***sum*** of all three, thereby introducing confounding variable bias. When examining liposomal bupivacaine's efficacy, it is scientifically appropriate to analyze studies involving other PAI cocktails. For example, femoral nerve blocks introduce confounders by acting over a different sensory distribution, as well as delay discharge due to quadriceps weakness. If you analyze the PAI group alone, there is no improvement (0.07 +/- 0.09 days, p = 0.48) in length of stay. We believe this finding would reach even greater significance if it included the data presented in our paper (2.32 +/- 0.53 liposomal bupivacaine versus 2.31 +/- 0.93 control, p = 0.93), which was included in your study (article #2) but left out of the analysis for unclear reasons.[2]

The meta-analysis claims improved pain scores on post-operative day (POD) 0 and 2, but day 1 scores were not different, which is illogical. This may be in part due to including pain scores from our paper in the POD 2 analysis; however, our pain scores were averaged from 24 hours after surgery to the time of discharge, as detailed in our methods, with some patients discharged on POD 3 [2]. Additionally, if you only compare treatment with other PAI studies, there is no difference on POD 1 (0.23 +/- 0.17, p = 0.20) or 2 (0.07 +/- 0.18, p = 0.69) in your analysis. Further, while your meta-analysis demonstrated a difference in PAI on POD zero (1.21 +/- 0.31, p = 0.00), the majority of data (74.5%) is from a single paper [3], which obviates the scientific credibility and proposed benefits of a meta-analysis. Additionally, authors of this particular study[3] have financial conflicts of interest, imparting bias. We appreciate Sing and co-authors[1] have no conflicts; however, author conflicts in the studies comprising the meta-analysis should have been considered and discussed.

We respectfully appreciate your effort on the important and controversial topic of liposomal bupivacaine's efficacy as a component of PAI; however, the study methodology has numerous critical flaws, which affect the results and render the conclusions invalid. Based on substantial increase in the cost and lack of scientifically proven efficacy, we do not advocate the use of liposomal bupivacaine in routine practice.

References

1. Singh, P.M., et al., *Role of Periarticular Liposomal Bupivacaine Infiltration in Patients Undergoing Total Knee Arthroplasty-A Meta-analysis of Comparative Trials.* J Arthroplasty, 2017. **32**(2): p. 675-688 e1.
2. Bagsby, D.T., P.H. Ireland, and R.M. Meneghini, *Liposomal bupivacaine versus traditional periarticular injection for pain control after total knee arthroplasty.* J Arthroplasty, 2014. **29**(8): p. 1687-90.
3. Bramlett, K., et al., *A randomized, double-blind, dose-ranging study comparing wound infiltration of DepoFoam bupivacaine, an extended-release liposomal bupivacaine, to bupivacaine HCl for postsurgical analgesia in total knee arthroplasty.* Knee, 2012. **19**(5): p. 530-6.